International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2018): 7.426

Surgical Outcome in Refractory Epilepsy due to Mesial Temporal Sclerosis: Analyses of 56 Consecutive Patients

Ahamed Sharief A SK[1], Suchanda Bhattacharjee[2], S A Jabeen[3], Rajesh Alugolu[4]

Department of Neurosurgery and Neurology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

Abstract: ***Objective: To analyse the surgical outcome in refractory epilepsy due to mesial temporal sclerosis at a tertiary care centre. Methods: post op longitudinal follow up of 56 consecutive patients operated on for drug resistant mesial temporal sclerosis. Results: The mean age of the present group was 25.4±8.06 years (4- 46 years). The most common age group was 20-30 years (62.5%). In this study, 62.5 % (n=35) of patients were males and rest were female. There were 41 patients (73.2%) with aura and 15 patients (26.8%) without aura in our study. In this study, there were 26 cases (46.4%) with dystonic posturing during seizure attack confirmed on video-EEG while it was absent in attendant description and video-EEG in 30 cases (53.6%). Most of the patients suffered for about 20 years prior to surgery. In this study, there were 42.8% (n=27) of Right MTS diagnosed on the basis of MRI alone, 51.8 %(n=29) were left MTS, 3.6 %(n=2) were negative for MTS study and 1.8 %(n=1) were bilateral MTS. In the present study, 24 patients showed Left IED (42.8%) and 23 cases showed Right IED (41%). Bilateral IED were seen in 7 cases (12.5%).In this study (n=56), mesial temporal sclerosis was reported in50 cases (89.3%) and in 6 cases (10.70%) MTS was associated with other pathology which could not be diagnosed preoperatively. In this study (n=56), 41% of the subjects were using ≤ 2 AED's and 59 % were using 3 or more AED's preoperatively. Outcome after a minimum follow up of 6 months was Engel grade I in 52 (92.8%) and Engel grade II in 4 cases (7.2 %). We observed that 37 subjects (66.1%) in this study had normal EEG which was done on 7th postoperative day and the rest (33.9%) showed abnormal EEG. 48 subjects (85.7%) had normal EEG at the end of 6 months after surgery and the rest (14.3%) had abnormal EEG. Most commonly seen postoperative complication was meningitis (4 cases) (7%). Conclusions: Anterior temporal lobectomy along with amygdalohippocampectomy is a standard treatment option for mesial temporal sclerosis in well selected cases. Oroalimentary automatisms classically remain most common semiology feature of mesial temporal sclerosis. There is no correlation between postoperative 7 th day EEG and 6 months EEG on surgical outcome. This study did not find any correlation between the duration of seizures prior to surgery, number of preop AED or any associated pathology along with mesial temporal sclerosis histologically with the surgical outcome.***

Keywords: mesial temporal sclerosis, epilepsy, anterior temporal lobectomy, amygdalo hippocampectomy, temporal lobe epilepsy, seizures

1. Introduction

Epilepsy is a worldwide health concern, accounting for 1% of the global burden of disease, equivalent to lung cancer in men and breast cancer in women (1). Approximately 20% to 40% of patients these patients who have medically intractable epilepsy account for 80% of the cost of treatment of epilepsy (2).

Temporal lobe epilepsy is the commonest form of partial epilepsy, and is amenable to surgical management. However, in India there exists a wide gap between the case load and surgical management. In India, with over 500,000 potential epilepsy surgery candidates, not more than 300 epilepsy surgeries per year are being undertaken today (3). Thus, enormous surgical treatment gap exists.

The surgical outcome may vary from complete cure (cessation of all anti-epileptic drugs) to complete control either on same number of pre surgical drugs in lower doses or less number of drugs.

The success of temporal epilepsy surgery depends on correct selection of candidates and epileptic zones. The temporal lobe epilepsy surgery is not without potential drawbacks which include verbal, visual and memory dysfunction.

This study is our endeavour to observe the outcomes following surgery for mesial temporal sclerosis following a standardised preoperative workup and surgical technique.

2. Methods

This was a retrospective and prospective observational study of patients with MRI and histologically verified MTS in a comprehensive epilepsy centre (Nizam's institute of medical sciences, Hyderabad) done between 2010 to 2016. Inclusion criteria were seizure semiology and abnormal EEG consistent with TLE and MRI determinants of hippocampal sclerosis. We excluded patients with a history of non-epileptic seizures or non-compliance, ambiguous EEG-findings and dual pathology on MRIscans. Furthermore, those who were not willing to participate in study and those who are not willing for follow up and those who lost to follow-up post surgically were excluded. Structural MRimaging was done on 1.5 Tesla MR Unit or 3 Tesla MR Unit. MRI was performed using SE, IR & GR sequences. T1W, T2W, FSEIR & 3D SPGR images (1.5mm slice thickness, with no intervening gap) were obtained in coronal planes. T2W images were obtained in axial planes. If there is any discordance, then inter ictal PET CT or Ictal SPECT was done depending on availability. MTS criteria were: (1) hippocampal atrophy demonstrated with coronal T1-weighted images, (2) signal hyper intensity within the hippocampus on T2- weighted or FLAIR images, and/or (3) disruption of the internal hippocampal architecture on T1

weighted images. Each patient had been evaluated with long-term video-EEG with surface and sphenoidal electrodes if necessary. Abnormal EEG was defined as interictal slowing; sharp slow wave, spike, and/or spike–slow wave; and a combination of these (4). In addition, focal ictal events characterized by temporal epileptiform fast activity; sharply contoured theta; spike and wave, rhythmic delta; or combinations of these were recorded from all patients. All patients had neuropsychological testing (5, 6).

Medical records were reviewed to establish seizure frequency and other details. In addition, previous AED treatment was documented. Seizure control was assessed based onfrequency prior to surgeryin comparison with 6 months after surgeryand expressed as ENGEL'S outcome grade.Patients with mesial temporal lobe epilepsy underwent the procedure of Anterior temporal lobe resection (ATL) + Amygdalohippocampectomy. A standard temporal craniotomy was done with bone exposed flush with the middle cranial fossa floor. Electro corticography done and Anterior temporal lobectomy was done with sparing of superior temporal gyrus. The length of temporal lobe resection will be 4 - 4.5 cm on the dominant side, and 4.5 – 5.5 cm, on non-dominant side. The resection limit was always anterior to Vein of Labbe. After Anterior lobectomy, temporal horn was opened, depth electrodes were placed for recordings and partial Amygdalectomy was performed. The choroidal fissure was opened and a partial hippocampectomy (about 2.5 – 3 cm) was done and the tissue was sent for histopathological examination. Seizure outcome was related to age, sex, MRIlesion side, semiology features, duration of epilepsy prior to surgery, and number of pre op AED's, post op 7 day EEG, post op 6 months EEG, and presence of dual pathology on histology. Statistical analysis was executed using EPI INFO version 7 (CDC, Atlanta). The level for statistical significance was set at $P < 0.05$.

3. Results

Fifty six patients (21 women, 35 men) met the inclusion criteria for our study. The average age in the study group was 25.4+_8.06 years. On the basis of the MRI investigations, 24patients had right, 29had left, 1 had bilateral pathology and 2 had no findings of mesial temporal sclerosis. There was a significantly higher proportion of left lesions in this studyand there was no significant correlation on outcome ($P < 0.2$).

In this study aura was noted in 41 (73.2%) cases, oroalimenatary automatisms seen in 47 (83.9%), dystonic posture noted in 26 (46.4%) cases, post ictal aphasia in 29 (52%) cases and post ictal nasal wiping observed 22 cases (39.3%). Sphenoidal electrodes placement was done in 6 (10.7%) cases. Inter ictal PET CT was done in 15 (27%) and Ictal SPECT was done in 4 (7%) cases. Inter ictal EEG showed right temporal IED in 23(37.5%), left temporal IED in 24(42.8%), bilateral temporal IED in 7 (12.5%) cases and normal EEG was seen in 2 cases (3.6%). 43 (59%) were using 3 or more than 3 anti epileptic drugs. Investigations and clinical data showed concordant data in 52 (93%) of cases. All the patients underwent standard anterior temporal lobectomy along with amygdalohppocampectomy. Histopathologic examination confirmed MTS in all cases. In 6 cases (10.6%) along with mesial temporal sclerosis there were other pathologies like FCD, microdysgenisis, ganglioglioma and microcalcifications which was identified on histology. Post ictal EEG done on 7 th day was abnormal in 19 (34%) and normal in 37 (66%) of cases. EEG done after 6 months was normal in 48(85.7%) and abnormal in 8 (14.3%) cases. 24 (43%) patients were free of all AED.

52 patients were garded as ENGEL's grade 1 and 4 as ENGEL's grade 2. There was no significant correlation between sex, duration of seizures prior to surgery, number of pre operative AED, presence or absence of aura or dystonic posture or post ictal nasal wiping on seizure outcome. The side of pathology whether right or left, histopathological examination finding of having dual pathology do not showed any effect on surgical outcome. Post op EEG done at 7 days (p=0.7) and 6 months (p=0.5) also do not have any influence on the surgical outcome.

4. Discussion

The mean age of the present group was 25.4±8.06 years (4-46 years). The most common age group was 20-30 years (62.5%). The mean age in Engel et al (2012) study was 34.3 years and in Wiebe et al (2001) study was 35.5 years (7). The mean age was slightly less in our study. We found no significant correlation between age at surgery and the surgical outcome (p = 0.2) which is akin to all the previous studies.

In this study, 62.5 %(n=35) of patients were males and rest were females. We found no significant relation between gender and the Engel outcome grade (p= 0.1). This is consistent with the results of Zhenxing et al. (p=0.274) (8) and Susanne et al. (p=0.379) wherein gender has no influence on surgical or seizure outcome (9).

There were 41 patients (73.2%) with aura and 15 patients (26.8%) without aura in our study. There was no significant correlation between aura and the ENGEL grade (p =0.2). Jeong et al. studied 93 cases of MTS and found that there is no significant effect of presence or absence of Aura on the ENGEL outcome grade (p=0.50) (10). In another study of 237 patients, Pooya et al. had not found any significance to the presence or absence of aura on the surgical outcomes (11).

In this study, there were 26 cases (46.4%) with dystonic posturing during seizure attack confirmed on video-EEG while it was absent in attendant description and video-EEG in 30 cases (53.6%). In our study, there was no significant correlation between dystonic posture and the outcome after surgery (p = 0.2). This parameter was earlier analysed by Janszky et al. and Susanne et al.. Janszky et al. found significant correlation of ictal dystonia with surgical outcome (p=0.039) (12). Susanne et al. study results were consistent with our results which proved that there was no effect of dystonic posturing during seizure attack on the surgical outcome (p=0.229) (9).

In this study, most of the patients suffered for about 20 years prior to surgery. We found no significance of the duration of

seizures prior to surgery and outcome (p=0.8), even on sub classifying them into subgroups. Our results are consistent with the Susanne et al. study results which showed no significance of the duration prior to surgery and the surgical outcome ENGEL grade (p=0.634) (9). However, Jeong et al. in their study in 93 patients showed a significant correlation between the duration of seizures and surgical outcome (0.04). They had shown that surgery done at around 14 ± 6.8 years of onset had better seizure outcomes as opposed to poorer outcomes when intervened at 19.5 ± 8.7 years (10).

In this study, there were 42.8% (n=27) of Right MTS diagnosed on the basis of MRI alone, 51.8 % (n=29) were left MTS, 3.6 %(n=2) were negative for MTS study and 1.8 %(n=1) were bilateral MTS. Eva Kumlien et al. have done a study in 83 cases of Mesial temporal sclerosis in which they have divided them into surgical group (n=36) and medical group (n=47). In surgical group they found right side predominance (n=24) over left. In addition they have concluded that the side of pathology will not have any influence on prognosis (p=0.7) (13). In the present study too, there was no significant correlation between the side of mesial temporal sclerosis and the outcome after the surgery (p=0.2). Similar results were described in earlier studies by Hardy et al. also (p=0.3) (14).

In the present study, 24 patients showed Left IED (42.8%) and 23 cases showed Right IED (41%). Bilateral IED were seen in 7 cases (12.5%). Inter ictal EEG was normal in 2 cases (3.6%) in the present study. We found no significance of Inter ictal EEG recordings on the surgical ENGEL outcome grade (p=0.29). Earlier studies by Jeong et al. (p=0.21) and Hardy et al. (p=0.48) had shown no significant correlation to interictal discharges and overall outcomes.

In this study (n=56), mesial temporal sclerosis was reported in 50 cases (89.3%) and in 6 cases (10.70%) MTS was associated with other pathology which could not be diagnosed preoperatively. There was no significance of pathological diagnosis on outcome in our study (p=0.4). Basu et al. in their clinicopathological study of complex partial seizures with mesial temporal sclerosis and dual pathology, concluded that dual pathology on HPE do not affect the outcome ENGEL grade (p = 0.068). (15)

In this study (n=56), 41% of the subjects were using ≤ 2 AED's and 59 % were using 3 or more AED's preoperatively. Most commonly used AED in this present study population was oxcarbazepine preoperatively. Out of them 24 (43%) of them were free of AED after surgery. Cukiert et al. (2009) also in his study of 212 subjects, showed that 68 (32 %) people were free of AED after surgery (16). We found no significance of number of preoperative AED and surgical outcome (p=0.7). Post operatively most of the cases are using AED's in lower doses and are in tapering stage.

Intra operatively we used ECOG in all cases. In 4 cases ECOG helped us to resect superior temporal gyrus where there were abnormal spikes.

We observed that 37 subjects (66.1%) in this study had normal EEG which was done on 7th postoperative day and the rest (33.9%) showed abnormal EEG. Radhakrishnan et al. studied 175 subjects of Mesial temporal sclerosis who underwent ATL and AH. They have done EEG on 7th postoperative day and the results did not show any significance of it on outcome (p=0.163). These results are consistent with the present study results which proved no significance of 7th postoperative day EEG on outcome (p=0.7). (17)

In the present study 48 subjects (85.7%) had normal EEG at the end of 6 months after surgery and the rest (14.3%) had abnormal EEG. There was no statistically significant effect of post op EEG on ENGEL outcome grade (p= 0.5). Janszky et al. have studied 184 patients with mesial temporal sclerosis to find out the predictors of surgical outcome. The followup was available for 171 (93%) at 6 months. Janszky et al. found no significance of EEG findings taken at 6 months after surgery and surgical outcome grade (12). These findings are consistent with our study results.

In this study most commonly seen postoperative complication was meningitis (4 cases) (7%). CSF leak from the wound site was noted in 3 cases. Hemiparesis as post op complication was seen in 3 cases, of which 2 improved completely with time during hospital stay. The other one case of hemiparesis was due to inadvertent injury to anterior choroidal artery, and the patient is having grip weakness and residual spasticity. A case developed transient inter nuclear ophthalmoplegia. Reason was unknown as the post op MRI did not showed any brainstem signal changes. In this series, we had two cases of post op homonymous hemianopia. Though we did not have done any objective tests for visual field examination, subjectively no patient complained of any disturbances in field of vision. We have not done neuropsychological tests after surgery in follow up. But none of these patients complained of any fresh memory disturbances post surgery.

Salanova et al. in their study on complications of temporal lobe epilepsy surgery quoted the incidence of hemiparesis and hemianopia as 0. 9% and 0.4%, respectively. They found difficulty with verbal memory (8.8%) and post op depression (5.5%) as most common of all post op complications. Our study also yielded similar results and 2 cases committed suicide because of depression on follow up of one and nine months. This highlights the importance of counselling and need for moral support to the patient and their family members in this long standing illness. Salanova et al. concluded that there is no effect of post op complications on the surgical outcome (18). We also had similar results in the present study (p=0.27).

5. Conclusions

Anterior temporal lobectomy along with amygdalohippocampectomy is a standard treatment option for mesial temporal sclerosis in well selected cases. Oroalimentary automatisms classically remain most common semiology feature of mesial temporal sclerosis. There is no correlation between postoperative 7 th day EEG and 6 months EEG on surgical outcome. This study did not find any correlation between the duration of seizures prior to surgery, number of preop AED or any associated pathology

along with mesial temporal sclerosis histologically with the surgical outcome.

6. Limitations

1) Pathological reports – we could not analyse different Sommer's sectors separately in histopathological examination, because of resection of Hippocampus in some cases was piece meal due to technical difficulties.
2) Post op visual fields – we have not done post op visual fields examination in post op period.
3) Per op ECOG – we have not analysed per op ECOG findings in the present study.
4) Post op neuropsychological assessment – we have not done post op neuropsychological evaluation in follow-up.

References

[1] Murray CJL, Lopez AD, eds. Global Comparative Assessment in the Health Sector; Disease Burden, Expenditures, and Intervention Packages. Geneva: World Health Organization, 1994.
[2] Engel J, Jr., McDermott MP, Wiebe S, Langfitt JT, Stern JM, Dewar S, et al. Early surgical therapy for drug-resistant temporal lobe epilepsy: a randomized trial. JAMA. 2012;307:922-30.
[3] Radhakrishnan K. Epilepsy surgery in India.Neurology India.2009; 57:4-6
[4] Gates, J. R. and Cruz-Rodriguez, R. Mesial temporal sclerosis: pathogenesis, and diagnosis, management. *Epilepsia* 1990; **31**: S55–S66.
[5] Wechsler, D. *Wechsler Adult Intelligence Scale*. San Antonio, The Psychological Corporation, 1981.
[6] Wechsler, D. *Wechsler Adult Intelligence Scale-revised*. San Antonio, The Psychological Corporation, 1981.
[7] Wiebe S, Blume WT, Girvin JP, Eliasziw M. Effectiveness, Efficiency of Surgery for Temporal Lobe Epilepsy Study G. A randomized, controlled trial of surgery for temporal-lobe epilepsy. The New England journal of medicine. 2001;345:311-8.
[8] Zhenxing sun, Huancong zuo, Dan yuan, Yaxing sun, Kai zhang, Zhiqiang cuiand Jin wang et al. Predictors of prognosis in patients with temporal lobe epilepsy after anterior temporal lobectomy. Exp Ther Med. 2015 Nov;10(5):1896-1902.
[9] Aull-Watschinger S, Pataraia E, Czech T, Baumgartner C. Outcome predictors for surgical treatment of temporal lobe epilepsy with hippocampal sclerosis. Epilepsia. 2008;49:1308-16.
[10] Jeong SW, Lee SK, Kim KK, Kim H, Kim JY, Chung CK et al. Prognostic factors in anterior temporal lobe resections for mesial temporal lobe epilepsy: multivariate analysis**.** Epilepsia. 1999 Dec;40(12):1735-9.
[11] Ali A. Asadi-Pooya, Maromi Nei, Ashwini Sharan, Michael R. Sperling, et al. Type of preoperative aura may predict postsurgical outcome in patients
[12] with temporal lobe epilepsy and mesial temporal sclerosis. Epilepsy & Behaviour 2015;50:98–100.
[13] Janszky J, Janszky I, Schulz R, Hoppe M, Behne F, Pannek HW, et al. Temporal lobe epilepsy with hippocampal sclerosis: predictors for long-term surgical outcome. Brain : a journal of neurology. 2005;128:395-404.
[14] Eva Kumlien, Robert C. Doss & John R. Gates. Treatment outcome in patients with mesial temporal sclerosis. Seizure 2002;11:413–417.
[15] Hardy SG, Miller JW, Holmes MD, Born DE, Ojemann GA, Dodrill CB, Hallam DK.et al. Factors predicting outcome of surgery for intractable epilepsy with pathologically verified mesialtemporal scl erosis. **Epilepsia.** 2003 Apr;44(4):565-8.
[16] P Basu, P Satishchandra, A Mahadevan, PN Jayakumar, SL Rao, PR Kavita, BA Chandra Mouli, SK Shankar, et al. A clinicopathological study of complex partial seizures with mesial temporal sclerosis and dual pathology: It's contribution in post-surgical outcome. *Neurology Asia. 2004; 9 (Supplement 1) : 148 – 149.*
[17] Cukiert A, Cukiert CM, Argentoni M, Baise-Zung C, Forster CR, Mello VA, Burattini JA, Mariani PP et al. Outcome after cortico amygdalo hippocampectomy in patients with refractory temporal lobe epilepsy and mesial temporal sclerosis without preoperative ictal recording. Epilepsia. 2009 Jun; 50 (6): 1371-6.
[18] 17.Radhakrishnan K, So EL, Silbert PL, Jack CR Jr, Cascino GD, Sharbrough FW, O'Brien PC et al. Predictors of outcome of anterior temporal lobectomy for intractable epilepsy: a multivariate study. Neurology. 1998 Aug;51(2):465-71.
[19] V. Salanova, O. Markand, and R. Worth. Temporal Lobe Epilepsy Surgery: Outcome, Complications, and Late Mortality Rate in 215 Patients. *Epilepsia, 2002;*43(2):170–174.